

Remarks

Claims 107, 124-126, 128, 130-137, 140-142, 149-154, 156-159 and 165-167 have been amended. Claims 143-148, 155, 160-164 and 168 have been canceled without prejudice or disclaimer. New claim 169 has been added. Support for the amendments to claims 124 can be found in the specification at, for example, pages 16-19, paragraph 57. Support for the amendments to claim 125 can be found in the specification at, for example, page 14, paragraph 53 and page 39, paragraph 89. Claims 107, 124-126, 128, 130-137, 140-142, 149-154, 156-159 and 165-167 have been amended to better recite the claimed invention. Support for new claim 169 can be found in the specification at, for example, page 12, paragraph 32. No new matter has been introduced by any of the amendments or by the new claim. After entry of the above amendments, claims 107, 124-142, 149-154, 156-159, 165-167 and 169 will be pending.

Allowable Subject Matter

Applicants note that the Examiner has allowed claim 107 and has stated that claims 155 and 156 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Rejection Under 35 U.S.C. 102(b)

Claims 124, 128, 129, 131 and 166 are rejected under 35 U.S.C. § 102(b) as being anticipated by the abstract of published application DD 280466A to Freistedt *et al.* ("Freistedt"). According to the Examiner, Freistedt teaches a method for sterilizing soft tissue implants wherein the tissue is contacted with propylene glycol, frozen, and irradiated.

Claim 124 has been amended to recite (a) the contacting of one or more tissues with propylene glycol and at least two other stabilizers selected from the recited group. At the very least, Freistedt does not teach or suggest these combinations of additives. Applicants therefore respectfully request that the grounds for this rejection be withdrawn and that claim 124 be found in a condition for allowance. Because claims 128, 129, 131 and 166 depend from claim 124 and therefore incorporate each of its features, Applicants request that the rejection of claims 128, 129, 131 and 166 also be withdrawn and that these claims also be found in a condition for allowance.

Rejection Under 35 U.S.C. 103(a): Freistedt

Claims 125, 140-143, 147, 160, 163, 164 and 167 are rejected under 35 U.S.C. §103(a) as being unpatentable over Freistedt. According to the Examiner, because Freistedt discloses that more than one radio-protectant may be used, a skilled artisan would have found it obvious to use additional radio-protectants in combination with propylene glycol to optimize treatment of the particular tissue.

Because claims 143, 147, 160, 163 and 164 have been canceled, the grounds for this rejection regarding these claims have been effectively mooted. As amended, claim 125 recites the contacting of one or more tissues with propylene glycol and irradiating with gamma radiation, wherein the total dose of gamma irradiation is at least about 35 kGy. In contrast, Freistedt does not teach or suggest any particulars regarding its disclosure of “sterilisation by radiation,” such as the type of radiation used, the rate of irradiation or the total dose of radiation. For at least these reasons, Freistedt does not teach or suggest claim 125. Applicants therefore request that the grounds for this rejection be withdrawn. Because claims 140-142 and 167 depend from claim 125 and therefore incorporate each of its features, Applicants request that the rejection of claims 140-142 and 167 also be withdrawn and that these claims also be found in a condition for allowance.

Although the Examiner has not rejected claim 124 over Freistedt, Applicants prospectively point out that claim 124 as amended recites (a) the contacting of one or more tissues with propylene glycol and at least two other stabilizers selected from DMSO and various specific polyols. Freistedt does not teach or suggest the use of more than one polyol in its recitation of a polyol and/or DMSO. The Examiner’s contention that because Freistedt describes the use of more than one radio-protectant, a skilled artisan would have found it obvious to use additional radio-protectants in combination with propylene glycol finds no support in Freistedt. Freistedt describes the use of one polyol with or without DMSO. There is no teaching that the use of additional polyols would provide greater tissue protection. In fact, Freistedt teaches away from the use of multiple polyols by describing, as a preferred composition, propylene glycol as a single radio-protectant. For at least these reasons, claim 124 and all claims that depend from claim 124 would not be obvious in view of Freistedt.

Rejection Under 35 U.S.C. 103(a): Freistedt in view of Kent

Claim 136 is rejected under 35 U.S.C. §103(a) as being unpatentable over Freistedt in view of U.S. Patent No. 6,171,549 to Kent (“Kent”). According to the Examiner, although Freistedt does not teach an irradiation dose rate, Kent describes a dose rate of 0.1-3.0 kGy/hr.

Neither claim 124 nor 125, as amended, is obvious over Freistedt for at least the reasons discussed above. Because Kent does not remedy the deficiencies in Freistedt as it pertains to claims 124 and 125, these claims cannot be obvious over Freistedt in view of Kent. Claim 136 alternatively depends from claims 124 and 125 and alternatively incorporates each of their features. Applicants therefore request that the grounds for this rejection be withdrawn.

Rejection Under 35 U.S.C. 103(a): Freistedt in view of Okrongly

Claims 148, 161, 162 and 165 are rejected under 35 U.S.C. §103(a) as being unpatentable over Freistedt in view of U.S. Patent No. 5,283,034 to Okrongly (“Okrongly”). According to the Examiner, although Freistedt teaches the use of DMSO, Freistedt does not teach the use of mannitol or trehalose. Okrongly is cited as teaching mannitol and trehalose as exemplary polyols for use as radio-protectants. The Examiner contends that it would have been obvious to a skilled artisan to use mannitol and trehalose as the polyols described by Freistedt.

Claims 148, 161 and 162 have been canceled, thereby rendering moot the Examiner’s rejection of these claims. Neither claim 124 nor 125, as amended, nor claim 165 which is dependent from these claims in the alternative, is obvious over Freistedt for at least the reasons discussed above. Because Okrongly does not remedy the deficiencies in Freistedt, Applicants request that the grounds for this rejection be withdrawn.

Rejection Under 35 U.S.C. 103(a): Freistedt in view of Peterson

Claims 137-139 are rejected under 35 U.S.C. §103(a) as being unpatentable over Freistedt in view of U.S. Patent No. 5,730,933 to Peterson (“Peterson”). According to the Examiner, although Freistedt does not teach a total irradiation dose, Peterson teaches irradiating biological materials so that they receive a dose of 30 kGy (3 mrad). In any case, the Examiner asserts that it is deemed within the purview of one in the art to optimize the total dose.

Neither claim 124 nor 125, as amended, nor claims 137-139 which are dependent from these claims in the alternative, is obvious over Freistedt for at least the reasons discussed above. Peterson teaches a maximum value of 30 kGy for irradiating biological materials. Because of the well-known sensitivity of the stability of biologically active materials to increases in the total amount of sterilizing radiation, a person of skill in the art would not be motivated by reading Peterson to irradiate such a material beyond a total dose of 30 kGy. In addition, Peterson discloses that sterilization of biologically

active compounds is difficult because of the significant impact of variations in the compounds' surrounding environment (see *e.g.*, col. 1, lines 47-53). Such disclosure would contradict the Examiner's assertion that modifications in the total amount of sterilizing radiation would be a simple optimization process. Because Peterson cannot not remedy the deficiencies in Freistedt, Applicants request that the grounds for this rejection be withdrawn.

Rejection Under 35 U.S.C. 103(a): Peterson in view of Freistedt

Claim 124, 126, 127 and 130-135 are rejected under 35 U.S.C. §103(a) as being unpatentable over Peterson in view of Freistedt. According to the Examiner, Peterson teaches sterilization of a biological material in the presence of a stabilizer "under standard sterilization conditions ... at an intensity and for a time duration sufficient to destroy substantially all of the microorganism contamination." The Examiner states that Peterson describes the material as being lyophilized or dried with drying agents and/or frozen and placed under a vacuum or inert gas. It is the Examiner's contention that it would have been obvious for a skilled artisan to use the propylene glycol stabilizer of Freistedt in the method of Peterson.

As discussed above, Peterson cannot not remedy the deficiencies in Freistedt. Claim 124, for example, requires the presence of propylene glycol and at least two other stabilizers. Claim 125 requires the presence of propylene glycol and a total sterilizing dose of gamma radiation of at least about 35 kGy. At the very least, Freistedt does not teach or suggest either of these features and so simply using propylene glycol in the described method of Peterson does not result in Applicants' invention. These same arguments apply to claims 126, 127 and 130-135 which depend from claims 124 and 125 in the alternative and thus alternatively incorporate each of the features of these claims. Applicants therefore request that the grounds for this rejection be withdrawn.

Rejection Under 35 U.S.C. 103(a): Peterson and Freistedt in view of Kent

Claim 136 is rejected under 35 U.S.C. §103(a) as being unpatentable over Peterson and Freistedt in view of Kent. According to the Examiner, Peterson teaches sterilization of a biological material in the presence of a stabilizer "under standard sterilization conditions ... at an intensity and for a time duration sufficient to destroy substantially all of the microorganism contamination." Although the Examiner acknowledges that Peterson does not specify the dose rate, Kent is cited as teaching a low dose rate of

0.1-3.0 kGy/hr. The Examiner contends that it would have been obvious to use the dose rate of Kent in the described method of Peterson.

Neither claim 124 nor 125, as amended, nor claim 136 which is dependent from these claims in the alternative, is obvious over Freistedt for at least the reasons discussed above. Because Peterson and Kent do not remedy the deficiencies in Freistedt, Applicants request that the grounds for this rejection be withdrawn.

Rejection Under 35 U.S.C. 103(a): Bateman

Claims 124, 125, 128, 129, 149, 150, 152-154, 163, 164 and 166 are rejected under 35 U.S.C. §103(a) as being unpatentable over WO 88/06043 to Bateman *et al.* ("Bateman"). According to the Examiner, Bateman teaches the sterilization of collagen wherein the collagen is stabilized with a water soluble polymer (propylene glycol) crosslinked with glutaraldehyde and then sterilized with gamma radiation. The Examiner contends that although Bateman does not disclose an example using polypropylene glycol (PPG) as the water soluble polymer, it would have been obvious to a skilled artisan.

Claims 163 and 164 have Claim 137 has been canceled, thereby rendering moot the Examiner's rejection of these claims. Bateman appears to be limited to water-soluble polymeric stabilizers, such as polypropylene glycol. Propylene glycol is a monomer and not the same as polypropylene glycol. Claims 124 and 125 recite the contacting of one or more tissues with propylene glycol. Bateman does not teach or suggest the use of propylene glycol. As such, Bateman cannot render claims 124 and 125 obvious. Claims 128, 129, 149, 150, 152-154 and 166 depend from claims 124 and 125 in the alternative and thus alternatively incorporate each of their features. Applicants therefore request that the grounds for this rejection as applied to claims 128, 129, 149, 150, 152-154 and 166 be withdrawn.

Rejection Under 35 U.S.C. 103(a): Horowitz in view of Freistedt

Claims 124, 144, 145, 150, 151, 157-159 and 168 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,712,086 to Horowitz *et al.* ("Horowitz") in view of Freistedt. With respect to claims 124, 144, 157-159 and 168, the Examiner states that Horowitz teaches a method of sterilizing biological materials combined with stabilizer mixtures and sensitizers such as purpurins, phthalocyanines, psoralens, *etc.* According to the Examiner, the stabilizer/scavenger can be mannitol and/or glycerol. The Examiner contends that it would have been obvious for a skilled artisan to have used

the propylene glycol and/or DMSO of Freistedt either alone or in combination with the stabilizers of Horowitz.

With respect to claim 145, the Examiner contends that it would have been obvious to optimize the concentration of mannitol used in the invention based upon treatment parameters such as degree of tissue contamination, type and amount of tissue and irradiation rate.

With respect to claims 150 and 151, the Examiner states that Horowitz discloses that it was known in the art to combine the treatment of a biological material with irradiation and a stabilizer mixture with a second virucidal treatment.

Claims 144, 145 and 168 have been canceled, thereby rendering moot the Examiner's rejection of these claims. Neither claim 124 nor 125, as amended, is obvious over Freistedt for at least the reasons discussed above. Horowitz does not remedy the deficiencies in Freistedt as it pertains to claims 124 and 125. For example, regarding claim 124, Horowitz does not teach or suggest the combination of propylene glycol and at least two other stabilizers selected from DMSO and several polyols. Regarding claim 125, Horowitz does not teach or suggest propylene glycol and a total sterilizing dose of gamma radiation of at least about 35 kGy. Therefore, claims 124 and 125 cannot be obvious over Horowitz in view of Freistedt. Applicants therefore request that the grounds for this rejection be withdrawn. Because claims 150, 151 and 157-159 depend from claims 124 and 125 in the alternative and thus alternatively incorporate their features, Applicants therefore request that the grounds for this rejection as applied to claims 150, 151 and 157-159 also be withdrawn.

Rejection Under 35 U.S.C. 103(a): Horowitz and Freistedt in view of Okrongly

Claim 146 is rejected under 35 U.S.C. §103(a) as being unpatentable over Horowitz and Freistedt in view of Okrongly. According to the Examiner, the combination of Horowitz with Freistedt teaches the use of oxygen scavengers but does not teach trehalose, while Okrongly teaches mannitol and trehalose. The Examiner contends that it would have been obvious to use trehalose as an exemplary polyol in the method of Horowitz.

Claim 146 has been canceled, thereby rendering moot the Examiner's rejection of this claim.

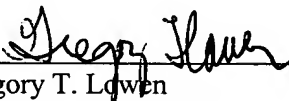
Conclusion

Upon consideration of the foregoing, it will be recognized that Applicants have fully and appropriately responded to all of the Examiner's rejections. Accordingly, all claims are believed to be in proper form in all respects and a favorable action on the merits is respectfully requested. The Examiner is invited to contact the undersigned with any questions or concerns that may prevent this requested allowance.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or to credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. 1.136(a)(3).

Dated: **February 25, 2005**
Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
Tel: 202-739-3000
Fax: 202-739-3001

Respectfully submitted
Morgan, Lewis & Bockius LLP



Gregory T. Lowen
Registration No. 46,882
Direct Tel: 202-739-5915